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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/539,107	06/15/2005	Tomasz Heyduk	102364	2295
27148	7590	12/18/2009	EXAMINER	
POL SINELLI SHUGHART PC 700 W. 47TH STREET SUITE 1000 KANSAS CITY, MO 64112-1802				BHAT, NARAYAN KAMESHWAR
1634		ART UNIT		PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/539,107	HEYDUK ET AL.	
	Examiner	Art Unit	
	NARAYAN K. BHAT	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 11 September 2009.
- 2a) This action is **FINAL**. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 109-117 and 119-142 is/are pending in the application.
- 4a) Of the above claim(s) 112-115,117 and 128-130 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 109-111,116,119-127 and 131-142 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ . |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>9/11/2009</u> . | 6) <input type="checkbox"/> Other: _____ . |

Continued Examination under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 11, 2009 has been entered.

Claim Status

2. Applicants have amended claims 109 and 127 and added claims 131-142. Claim amendments have been reviewed and entered. Claims 109-117 and 119-142 are pending in this application. Applicants arguments filed on September 11, 2009 have been fully considered and addressed following rejections. Previous rejections under 35 USC 102 (b) and 103 (a) not reiterated below have been withdrawn. Applicant's acknowledgement of the interview summary filed by the Examiner is noted.

3. Claims 112-115, 117 and 128-130 were withdrawn from further consideration pursuant to 37 CFR 1.142(b) in the reply filed on April 16, 2007 and made final on July 2, 2008.

4. Claims 109-111, 116, 119-127 and 131-142 are under prosecution.

Declarations

5. The declaration under 37 CFR 1.132 filed by Dr. Heyduk on September 11, 2009 to highlight the free energy of association requirement for the claimed sensor and higher sensitivity relative to that of Baez et al is noted. The claim amendments filed September 11, 2009 define over Baez et al (USPGPUB 20020051986).

However, as discussed below, the declarations and support documents illustrating unexpected results over the teachings of Baez et al are not sufficient to overcome the instant rejections set forth in this office action.

Dr. Heyduk presented unexpected results from the sensor comprising free energy for association for R3 and R7 nucleic acid sequences comprising:

a) nucleic acid sequence “ATGAGC”, b) fluorescein and CY5 labeled anti-C peptide antibodies, c) buffer comprising 20 mM Tris, 100 mM NaCl, 10 mM EDTA and 0.25 mg/ml BSA and d) 25⁰C (Declarations, section i).

However, nucleic acid sequence “ATGAGC”, labeled antibodies, Tris buffer, EDTA and BSA are not claimed composition. Furthermore, it is not clear which of these components contribute or inhibit or control the unexpected signal production or the R3/R7 pair having free energy of association between about 5.5 kcal/mole and 8.0 kcal/mole as asserted by Dr. Heyduk (Declarations, sections ii and iii).

However, claims as recited have broader scope, with respect to temperature from about 21⁰C to about 40⁰C and salt concentration from about 1 mM to about 100 mM. Therefore unexpected results illustrated in the declaration are not commensurate with the scope of the claim. Furthermore, declarations regarding sensor sensitivity are

based on the calculation of free energy of association for nucleic acid sequences from the sensor of Baez et al are not enough because of the reference of Baez et al has been withdrawn because of claim amendments.

As described below in section 11, Egholm et al teaches a sensor comprising R3/R7 sequences complementary over the entire length of the nucleotide sequence having a free energy of association of 6.08 kcal/mol at 37⁰C and 100 mM salt concentration as defined by SantaLucia. Therefore, the declarations and the supporting documents illustrating unexpected results over the teachings of Baez et al are not sufficient to over come the instant rejections set forth in this office action.

Objection

6. Previous objection to claim 118 have been withdrawn in view of cancellation of said claim.

Claim Interpretation

35 U.S.C. 112, Sixth Paragraph

7. Claims 109, 127 and 131 are written using means-plus- function language. 'The M PEP § 2181-2184 provides guidance for claim evaluation and examination under 35 U.S.C. 112, Sixth Paragraph as set forth below:

The USPTO must apply 35 U.S.C. 112, sixth paragraph in appropriate cases, and give claims their broadest reasonable interpretation, in light of and consistent with the written description of the invention in the application. See Donaldson, 16 F.3d at

1194, and 29 USPQ2d at 1850 (stating that 35 U.S.C. 112, sixth paragraph “merely sets a limit on how broadly the PTO may construe means-plus-function language under the rubric of reasonable interpretation”. The Federal Circuit has held that applicants (and reexamination patentees) before the USPTO have the opportunity and the obligation to define their inventions precisely during proceedings before the PTO. See *In re Morris*, 127 F.3d 1048, 1056-57, 44 USPQ2d 1023, 1029-30 (Fed. Cir. 1997).

A claim limitation will be presumed to invoke 35 U.S.C. 112, sixth paragraph, if it meets the following 3-prong analysis:

- (A) the claim limitations must use the phrase “means for” or “step for;”
- (B) the “means for” or “step for” must be modified by functional language; and
- (C) the phrase “means for” or “step for” must not be modified by sufficient structure, material, or acts for achieving the specified function. (see MPEP § 2181(I)).

8. The limitation of “a detection means” in claims 109, 127 and 131 do not meet the first and third criteria of the 3-prong analysis, because “means” is modified by sufficient structure for achieving the function, i.e., association of R3 and R7. Therefore claims 109, 127 and 131 will not be limited to the “detection means” disclosed in the specification.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

- (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 109-110, 119-127, 131-132 and 135-142 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Egholm et al (USPN 6,451,588 issued Sep. 17,2002) in view of Weston et al (USPN 6,391,593 issued May 21, 2002). The free energy calculation is defined by SantaLucia (PNAS, 1998, 95, 1460-1465).

Regarding claims 109 and 131, Egholm et al teaches a molecular biosensor having first probe 12 and a second probe 14 (i.e., constructs) each having structural features of R1-R2-R3 and R5-R6-R7 respectively as discussed below.

It is noted that claim 131 recite same structural components recited in claim 109 except for R3 and R7 do not require having complementary nucleotide sequence over the length of the nucleotide sequence.

Regarding structural component R1, Egholm et al teaches a first probe 12 comprising a first portion 16 that binds to a first region 18 on the target molecule 20 (Fig. 1A, column 6, lines 35-41). Instant specification defines epitope binding agent as an aptamer comprising nucleic acid sequence (USPGPUB, paragraph 0054). The first portion 16 of Egholm et al comprising the nucleic acid sequence (column 6, section V.2)

is the epitope binding agent as defined in the instant specification (USPGPUB, paragraph 0054).

Regarding structural component R5, Egholm et al teaches a second probe 14 comprising a first portion 22 that binds to a second region 24 on the target molecule 20 (Fig. 1, column 6, lines 41-43). The first portion 22 of Egholm et al comprising the nucleic acid sequence (column 6, section V.2) is the epitope binding agent as defined in the instant specification (USPGPUB, paragraph 0054).

Regarding structural component R2, Egholm et al teaches ethyleneoxy (i.e., non-nucleic acid) flexible linker 30 to attach the first portion 16 (i.e., R1) to second portion 26, i.e., R3 of the first probe 12 (Fig. 1A, column 9, lines 25 -40).

Regarding structural component R6, Egholm et al teaches ethyleneoxy (i.e., non-nucleic acid) flexible linker 30 to attach the first portion 22 (i.e., R5) to second portion 28, i.e., R7 of the second probe 14 (Fig. 1A, column 9, lines 32 -40).

Regarding structural components R3 and R7, Egholm et al teaches that first probe 12 comprises second portion 26 (i.e., R3) and the second probe 14 comprises second portion 28 (i.e., R7) and further teaches that the second portion 26 (i.e., R3) and 28 (i.e., R7) comprises nucleotide sequences that are complementary over entire length of the nucleotide sequences (Figs. 1A and 7 and column 6, section V.2 and column 8, lines 33-38). Egholm et al also teaches a temperature of 37⁰C (Example 2 and column 20, lines 16-17) and salt concentration of 100 mM (Example 2 and column 20, line 13). A temperature of 37⁰C is within the range from about 21⁰C to about 40⁰C as claimed.

Egholm also teaches that the R3 and R7 sequence comprises TGACTGAC and complementary ACTGACTG sequences forming a duplex at 100 mM salt concentration and at a temperature of 37⁰C (Fig. 1A and Example 2) and has a free energy of association of about 6.08 kcal/mol as defined by SantaLucia (Table 1, column labeled as Blake). The free energy of 6.08 kcal/mole is in the range from about 5.5 kcal/mole to 8.0 kcal/mole as claimed.

Regarding structural components R4 and R8, Egholm et al teaches that the probes are labeled with labeling moieties for detecting the target by FRET (column 9, section V.5, Column 11, lines 13-35). Egholm et al do not teach R4 and R8 together comprise a detection means such that when R3 and R7 associate detection signal is produced.

Teachings of Egholm et al of R3 and R7 are a pair of complementary nucleotide sequences having a free energy of association of about 6.08 kcal/mol at 100 mM salt concentration and at a temperature of 37⁰C encompasses the limitation of claim 131.

Regarding claims 110 and 132, Egholm et al teaches that the target molecule is a nucleic acid 20 (Fig. 1A and column 2, line 10).

Regarding claims 119, 120, 135 and 136, as described above, Egholm et al teaches that the first probe 12 comprises flexible linker 30 (i.e., R2) forms a covalent bond with each of first portion 16 (i.e., R1) and second portion 26, i.e., R3 (Fig. 1A) and further teaches that the second probe 14 comprises flexible linker 30 (i.e., R2) forms a covalent bond with each of first portion 22 (i.e., R5) and second portion 28, i.e., R7 (Figs. 1A and 7 and column 6, section V.2). Egholm et al also teaches that the R2 and

R6 non-nucleic acid linker reduces the strain associated with the first and second probe (column 12, lines 47-53), thereby stabilizing the association of R3/R7. The claimed free energy of the formed bonds from about 12.0 kcal/mole to about 16.5 kcal/mole is an obvious variant of the free energy of the association of R3/R7 taught by Egholm et al.

Regarding claims 121, 123, 137 and 139, Egholm et al teaches the ethylene oxy flexible (PEG) linker 30 (i.e., R2 and R6) to couple first portion of the probe to the second portion of the probe (Fig. 1A and column 9, section V.4) and is the bifunctional chemical cross linker as defined in the instant claim 123.

Regarding claim 122 and 138, Egholm et al teaches that the ethyleneoxy flexible (PEG) linker 30 (i.e., R2 and R6) comprises up to six ethyleneoxy units (column 9, section V.4, lines 37-39) which encompasses at least 9 angstrom units (C-C bond length = 1-5 angstrom units). It is also noted that the claim recitation of R2 and R6 from Zero to 500 angstrom in length, indicates that R2 and R6 are not needed when the length of the bifunctional cross linker is zero angstrom.

Regarding claim 124 and 140, Egholm et al teaches that the R3 and R7 are 8 nucleotide in length (Fig. 7 and Example 1), which is within the range from about 4 to about 15 nucleotide in length as claimed.

Regarding claim 125 and 141, Egholm et al teaches that the labels on the nucleic acid probes comprise acceptor and donor molecules that transfer energy producing a detectable signal (column 11, lines 27-35).

Regarding claim 126 and 142, Egholm et al teaches FRET (column 11, lines 14-17).

Regarding claim 127, Egholm et al teaches a molecular biosensor having first probe 12 and a second probe 14 (i.e., constructs) each having structural features of R1-R2-R3 and R5-R6-R7 respectively as discussed below.

Regarding structural component R1, Egholm et al teaches a first probe 12 comprising a first portion 16 that binds to a first region 18 on the target molecule 20 (Fig. 1A, column 6, lines 35-41). Instant specification defines epitope binding agent as an aptamer comprising nucleic acid sequence (USPGPUB, paragraph 0054). The first portion 16 of Egholm et al comprising the nucleic acid sequence, i.e., an aptamer (column 6, section V.2) is the epitope binding agent as defined in the instant specification (USPGPUB, paragraph 0054).

Regarding structural component R5, Egholm et al teaches a second probe 14 comprising a first portion 22 that binds to a second region 24 on the target molecule 20 (Fig. 1, column 6, lines 41-43). The first portion 22 of Egholm et al comprising the nucleic acid sequence, i.e., an aptamer (column 6, section V.2) is the epitope binding agent as defined in the instant specification.

Regarding structural component R2, Egholm et al teaches ethyleneoxy (i.e., non-nucleic acid) flexible linker 30 attaching the first portion 16 (i.e., R1) to second portion 26, i.e., R3 of the first probe 12 by covalent bond (Fig. 1A, column 9, section V.4 and lines 25 -40). Egholm et al also teaches that the ethyleneoxy flexible (PEG) linker 30 comprises up to six ethyleneoxy units (column 9, section V.4, lines 37-39) which encompasses at least 9 angstrom units (C-C bond length = 1-5 angstrom units). It is

also noted that the claim recitation of R2 from Zero to 500 angstrom in length, indicates that R2 is not needed when the length of the bifunctional cross linker is zero angstrom.

Regarding structural component R6, Egholm et al teaches ethyleneoxy (i.e., non-nucleic acid) flexible linker 30 attaching the first portion 22 (i.e., R5) to second portion 28, i.e., R7 of the second probe 14 by covalent bond (Fig. 1A, column 9, section V.4 and lines 25 -40). Egholm et al also teaches that the ethyleneoxy flexible (PEG) linker 30 comprises up to six ethyleneoxy units (column 9, section V.4, lines 37-39) which encompasses at least 9 angstrom units (C-C bond length = 1-5 angstrom units). It is also noted that the claim recitation of R6 from Zero to 500 angstrom in length, indicates that R6 is not needed when the length of the bifunctional cross linker is zero angstrom.

Regarding structural components R3 and R7, Egholm et al teaches that first probe 12 comprises second portion 26 (i.e., R3) and the second probe 14 comprises second portion 28 (i.e., R7) and further teaches that the second portion 26 (i.e., R3) and 28 (i.e., R7) comprises nucleotide sequences that are complementary over entire length of the nucleotide sequences (Figs. 1A and 7 and column 6, section V.2 and column 8, lines 33-38). Egholm et al also teaches a temperature of 37⁰C (Example 2 and column 20, lines 16-17) and salt concentration of 100 mM (Example 2 and column 20, line 13). A temperature of 37⁰C is within the range from about 21⁰C to about 40⁰C as claimed.

Egholm also teaches that the R3 and R7 sequence comprises TGACTGAC and complementary ACTGACTG sequences forming a duplex at 100 mM salt concentration and at a temperature of 37⁰C (Fig. 1A and Example 2) and has a free energy of

association of about 6.08 kcal/mol as defined by SantaLucia (Table 1, column labeled as Blake). The free energy of 6.08 kcal/mole is in the range from about 5.5 kcal/mole to 8.0 kcal/mole as claimed.

Regarding structural components R4 and R8, Egholm et al teaches that the probes are labeled with labeling moieties for detecting the target by FRET (column 9, section V.5, Column 11, lines 13-35).

As described above, Egholm et al teaches nucleic acid probes comprising donor and acceptor label for FRET (column 11, lines 27-35). Egholm et al do not teach R4 and R8 together comprise a detection means such that when R3 and R7 associate detection signal is produced. However nucleic acid probes carrying detection signals were known in the art at the time of the claimed invention was made as taught by Weston et al.

Weston et al, like Egholm et al teaches a biosensor comprising multipartite probes, wherein each probe having a first portion (i.e., epitope binding agent) and a flexible linker coupling the first and the second portion (Fig. 1, column 3, lines 24-43). Weston et al also teaches that the one of the probe carries the FAM label at its 5' end and the other probe carries TAMRA label at its 3' end such that when two probes hybridized together with the target nucleic acid probes are positioned adjacent to one another and FRET occurs (column 10, lines 43-49, limitations of claims 125 and 141).

Combined teachings of Egholm et al and Weston et al encompass two probes having first portions binding to different regions of the target bringing together second portions with two label for energy transfer reaction, thereby teaching R4 and R8 together comprise a detection means such that when R3 and R7 associate a detection

signal is produced. Therefore claimed molecular biosensor having two constructs comprising R1-R2-R3-R4 and R1-R2-R3-R4 is obvious over Egholm et al and Weston et al.

Weston et al also teaches multipartite probe having donor and acceptor molecule adjacent to one another reduces the background and increases the specificity of target detection thereby increasing the signal to noise ratio of target detection (column 8, lines 57-61).

It would have been prima facie obvious to one having the ordinary skill in the art at the time the invention was made to modify the probes of Egholm et al with probes carrying donor acceptor labels at 5 and 3' end with a reasonable expectation of success.

An artisan would have been motivated to modify the probes of Egholm et al with the expected benefit of reducing the background and increasing the specificity of target detection thereby increasing the signal to noise ratio of target detection as taught by Weston et al (column 8, lines 57-61).

12. Claims 109, 111, 116, 131, 133 and 134 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Egholm et al (USPN 6,451,588 issued Sep. 17, 2002) in view of Weston et al (USPN 6,391,593 issued May 21, 2002) as applied to claims 109 and 131 as above and further in view of Baez et al (USPGPUB 20020051986 published May 2, 2002).

Claims 111 and 116 are dependent from claim 109. Claims 133 and 134 are dependent from claim 131. Teachings of Egholm et al and Weston et al regarding claims 109 and 131 are described above in section 12.

Regarding claims 111 and 133, Egholm et al and Weston et al do not teach target molecule is a protein or polypeptide.

Regarding claims 116 and 134, Egholm et al and Weston et al do not teach R1 and R5 are each antibodies.

However, antibody as an epitope binding agent was known in the art at the time of the claimed invention was made as taught by Baez et al.

Baez et al teaches a molecular biosensor having two nucleic acids constructs comprising a nucleic acid reporter conjugate A comprising a first antibody (i.e., R1) binding to a first epitope on a target molecule (Fig. 1, first Antibody - shown as lambda shape in A, Target B, first Epitope C1 paragraphs 0017, 0023 and 0089). Baez et al also teaches another nucleic acid reporter conjugate A1 comprising a second antibody (i.e., R5) binding to a second epitope on a target molecule (Fig. 1, second Antibody – shown as lambda shape in A1, Target B, second Epitope C2, paragraphs 0017, 0023 and 0089).

Regarding claims 111 and 133, Baez et al teaches that the target molecule is a protein or polypeptide (paragraph 0052).

Baez et al also teaches antibody nucleic acid reporter conjugate improves the ratio of analyte specific signal to analyte non-specific background signal thereby enhancing analyte detection at very low concentration (paragraph 0017).

It would have been prima facie obvious to one having the ordinary skill in the art at the time the invention was made to modify the epitope binding agent of Egholm et al with the antibody epitope binding agent of Baez et al with a reasonable expectation of success.

An artisan would have been motivated modify the epitope binding agent of Egholm et al with the expected benefit of improving the ratio of analyte specific signal to analyte non-specific background signal thereby enhancing analyte detection at very low concentration as taught by Baez et al (paragraph 0017).

Double Patenting

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claims 109-111, 116, 119-127 and 131-142 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11 of copending Application 11/836,339 in view of Egholm et al (USPN 6,451,588 issued Sep. 17, 2002) and Weston et al (USPN 6,391,593 issued May 21, 2002). Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons.

Regarding instant claims 109, 127 and 131, the claim 1 of copending '339 application is drawn to a molecular biosensor comprising R47-R48-R49-R50 and R51-R52-R53-R54 and has structural features of epitope binding agent (R47 and R51), flexible PEG linkers (R48 and R52), complementary nucleic acid sequences (R49 and R53) and detection means (R50 and R53). Additional structural limitation of flexible linkers, nucleic acid composition and detection means of instant claim 127 are recited in claims 2-6 of the copending '339 application. The molecular biosensor of the claim 1 of copending '339 application differs from the instant claim 1, 127 and 131 molecular biosensor in the epitope binding agent structural features, specifically, the epitope binding agent, R51, does not bind to a target molecule (as required by claims 1, 127 and 131).

However, epitope binding agents binding to the first and second epitope on the target molecule were known in the art at the time of the claimed invention was made as taught by Egholm et al, and Weston et al as described above in section 11 for increasing the signal to noise ratio of target detection.

It is also noted that Egholm et al and Weston et al further discloses additional limitations required by instant dependent claims 110-111, 116, 119-126 and 132-142 as described in detail in this office action in section 12. Therefore the embodiments of claims 109-111, 116, 119-126 and 132-142 are also obvious for the same reasons given above for instant claims 109, 127 and 131 obvious over claims 1-11 of the '339 copending application in view of Egholm et al and Weston et al.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

15. Claims 109-111, 116, 119-127 and 131-142 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-18 of copending Application 11/836,333 in view of Egholm et al (USPN 6,451,588 issued Sep. 17, 2002) and Weston et al (USPN 6,391,593 issued May 21, 2002). Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons.

Regarding instant claims 109, 127 and 131, the claim 1 of copending '333 application is drawn to a molecular biosensor comprising R24-R25-R26-R27 and R28-R29-R30-R31 and has structural features of epitope binding agent (R24 and R28), flexible PEG linkers (R25 and R29), nucleic acid sequences (R26 and R30) and detection means (R27 and R31), wherein epitope binding agents R24 and R28 bind to the first and second epitopes on the target molecule and further comprises of antibody (claim 5 of the copending '333 application, limitations of instant claim 127). Additional

structural limitation of flexible linkers, nucleic acid composition and detection means of instant claim 127 are recited in claims 2, 6-8 of the copending ‘333 application.

Biomolecular sensor of claims 1 and 5-8 of copending ‘333 application differs from the molecular biosensor of instant claim 109 and 127 in that the R26 and R30 nucleic acids are not complementary to each other.

However, nucleic acid structure complementary to each other were known in the art at the time of the claimed invention was made as taught by Egholm et al and Weston et al as described above in section 11 for increasing the signal to noise ratio of target detection.

It is also noted that Egholm et al and Weston et al further discloses additional limitations required by instant dependent claims 110-111, 116, 119-126 and 132-142 as described in detail in this office action in section 12. Therefore the embodiments of claims 109-111, 116, 119-126 and 132-142 are also obvious for the same reasons given above for instant claims 109, 127 and 131 obvious over claims 1-18 of the ‘333 copending application in view of Egholm et al and Weston et al.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to remarks from Applicants

Rejections under 35 U.S.C. § 102(b)

16. Applicant's arguments filed September 11, 2009 with respect to claims 109-111, 116, 119-122 and 124-127 as being anticipated by Baez et al have been fully

considered (Remarks, pgs. 11-17). Applicant's arguments regarding teachings of Baez et al are persuasive and hence rejection is withdrawn.

Rejections under 35 U.S.C. § 103(a)

17. Applicant's arguments filed September 11, 2009 with respect to claims 109 and 123 as being unpatentable over Baez et al and Zalipsky et al have been fully considered (Remarks, pgs. 17-20). Applicant's arguments regarding teachings of Baez et al are persuasive and hence rejection is withdrawn.

Double Patenting

18. Applicants have not presented arguments traversing the obviousness-type double patenting rejection. Therefore, provisional obviousness-type double patenting rejection of instant claims 109-111, 116, 119-127 and 131-142 over claims 1-11 of '339 co-pending Application and over claims 1-18 of '333 copending Application in view of combination of references are maintained.

Conclusion

19. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Narayan K. Bhat whose telephone number is (571)-272-5540. The examiner can normally be reached on 8.30 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571)-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Narayan K. Bhat/

Examiner, Art Unit 1634

/BJ Forman/

Primary Examiner, Art Unit 1634